RESEARCH NEWS AND TRENDS FROM THE NATIONAL INSTITUTE ON DRUG ABUSE

NIDA Notes

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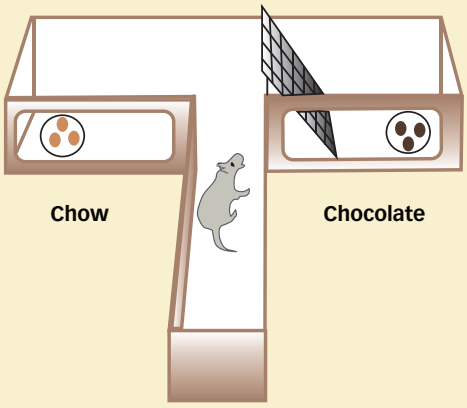
Neuropeptide Promotes Behaviors Tied to Addiction and Overeating

Orexin receptor-blocking medications might treat both cocaine abuse and unhealthy eating.

BY LORI WHITTEN,
NIDA Notes Staff Writer

Three teams of NIDA-funded investigators have implicated the neuropeptide orexin (also called hypocretin) in responses that can foster the transition from casual cocaine use to regular abuse and relapse. Two of the teams also tied orexin to eating high-caloric foods that can promote obesity. The findings bode well for a strategy of treating drug abuse and overeating with medications that inhibit orexin signaling.

A RAT'S CHOICE: FREE CHOW OR WORK FOR CHOCOLATE? In an effort-based task, rats could obtain pellets of chow by simply walking to the end of one arm of the structure, but they had to climb over a wire-mesh barrier to get to pellets of high-fat chocolate. Most rats went over the barrier, but they did so less often when they had received SB334867, a compound that blocks receptors for the neuropeptide orexin.



Adapted from *Cerebral Cortex* 17(2):251–260, 2007.

WORKING HARDER FOR COCAINE

Dr. Stephanie Borgland of the University of British Columbia (UBC), Dr. Antonello Bonci of the University of California, San Francisco (UCSF), and colleagues demonstrated that orexin sustains cocaine seeking when access to the drug becomes difficult. Their findings suggest that orexin raises the likelihood that a person who has started using cocaine will continue—and possibly become addicted—despite mounting financial and social costs of obtaining and using the drug.

The UBC–UCSF team conducted progressive ratio trials to investigate whether rats with normal orexin signaling will persist in cocaine seeking after rats with blocked signaling give up. At the start of a trial, animals could self-administer 0.5 mg/kg of the drug by pressing a lever once, but thereafter each dose required more presses than the previous one (see "Animal Experiments in Addiction Science," *NIDA Notes,* Volume 20, Number 5, page 11). The researchers gave some rats an inert substance and injected others with a compound, SB334867, that interrupts orexin signaling by blocking the neuropeptide from activating the orexin-1 receptor. The first group pressed the

[*Continued on page 12*]

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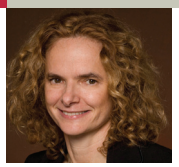
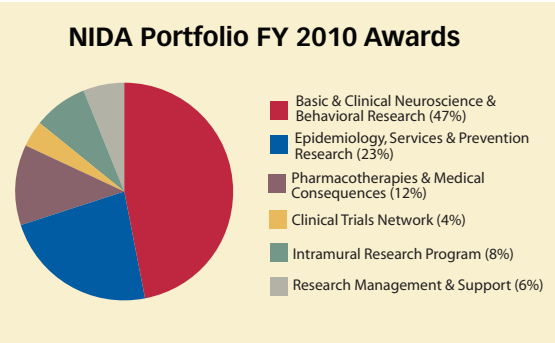


NIDA's Funding Priorities To Remain Constant

In these tough budget times, it is not surprising that rumors will take hold about where we will direct our funding priorities at NIDA. To counter with facts, I would like to reassure all of our research grantees that our priorities remain the same—that is, a focus on prevention, treatment, and HIV—and that no one aspect of NIDA's multilayered research portfolio will be neglected to the enhancement of others. It has been rumored, for example, that medications development will capture an inequitable portion of our budget; however, this is not true. While medications development is a critical piece of the research we fund, particularly since pharmaceutical companies have been reluctant to invest, it reflects only 12 percent of our total budget, a rate relatively unchanged over the last several years. Please know that I appreciate the work of all of our grantees and am keenly aware that it takes all of their varied contributions to carry out NIDA's mission "to lead the Nation in bringing the power of science to bear on drug abuse and addiction." ■



SPECIAL ANNOUNCEMENT

NIDA's Journal Will Move to Biomed Central

NIDA's award-winning peer-reviewed journal, *Addiction Science & Clinical Practice* (*AS&CP*), has been acquired by Biomed Central, a large science, technology, and medicine publisher that pioneered the open-access model. At its new home, the journal will continue to be freely available on the Web but will no longer appear in a print edition.

Taking over as editors will be Richard Saitz, M.D., M.P.H., and Jeffrey Samet, M.D., M.A., M.P.H. The highly regarded NIDA-funded researchers and clinicians are based at the Clinical Addiction Research and Education (CARE) Unit at Boston Medical Center, Boston University School of Medicine, and Boston University School of Public Health.

Dr. Saitz and Dr. Samet are soliciting clinically relevant research articles to appear after NIDA publishes its final issue later this summer. Readers and potential authors can find detailed information regarding the editors' aims and scope for the journal, sought-for article types, and a list of internationally known editorial board members at *www.ascpjournal.org*.

AS&CP, founded by NIDA in 2002, has been the Institute's primary printed vehicle for fostering dialogue between researchers and clinicians. Edited by David Anderson, M.S., since its inception, *AS&CP* reaches 34,000 subscribers with features written by top experts of bench and clinic. Readers have especially appreciated "response panels" that have followed most articles, in which professionals representing diverse perspectives in the field discuss the content and subject area. Enhanced by copious high-quality color graphics, with selected articles translated into several languages, the journal has won multiple editorial awards and has been indexed in Medline since 2004. ■

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Treatment Dropout Linked With Elevated Stress Response

A stress-related biological marker in saliva can predict how long a drug user will remain in treatment. In a recent study of men and women entering a residential treatment center, scientists measured salivary cortisol—a hormone that is released in stressful situations and is associated with the "fight or flight" response—just before participants performed two laboratory tasks designed to induce stress. The researchers repeated the measurement immediately after task completion and then at three 10-minute intervals.

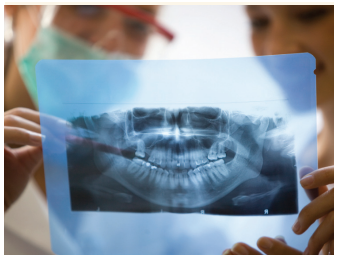
Prior to the tasks, cortisol levels were similar for the 21 patients who subsequently dropped out of treatment and the 81 patients who completed it. Thirty minutes after the stressor, however, individuals who later dropped out of treatment had cortisol levels that were 3.5 times higher than those of individuals who remained in treatment for their entire 30- or 60-day contract duration. Further, for each unit of increase in cortisol after the tasks, there was a four-fold increase in risk for dropping out of the treatment program on any given day. The findings also confirmed that participants who had indicated on a standard questionnaire that they had trouble dealing with stressful situations were most likely to leave treatment prematurely. Study leader Dr. Stacey B. Daughters of the University of Maryland suggests that patients with problems tolerating stress may benefit from evidence-based treatments that focus on coping with negative emotions.

> Drug and Alcohol Dependence 105(3):202–208, 2009.

Drugs Contribute to High Rates of Sexually Transmitted Diseases Among Juvenile Offenders

In a study of 948 newly arrested youths undergoing criminal justice intake processing in Tampa, Florida, more than 19 percent of girls and 11 percent of boys tested positive for chlamydia, gonorrhea, or both infections. Dr. Richard Dembo and colleagues from the University of South Florida, Tampa, and Temple University, Philadelphia, found correlations between the youths' prevalence of these sexually transmitted diseases (STDs) and their cocaine and marijuana use, as confirmed by urine tests. The youths' responses to a survey provided additional evidence of a prominent role for drug abuse as a risk factor for STDs. Sexual activity while using noninjected drugs was, at 8 percent, the second most commonly reported risk factor among boys and, at 9 percent, the third most common among girls. The primary STD risk factor for both sexes, at 21 percent for boys and 24 percent for girls, was heterosexual intercourse without a condom; the second most common for girls, at 10 percent, was sexual assault. The researchers say that their study results indicate a need to offer STD testing and treatment to all newly arrested juveniles, especially girls, to improve the health of a population that often lacks access to health care.

> Journal of Behavioral Medicine 32(2):129–141, 2009.



Methamphetamine Abuse Undermines Dental Health

Clinicians have long observed that methamphetamine users often have extreme dental decay. Now researchers have, for the first time, provided scientific evidence of this condition and shed light on how the method of drug administration influences dental disease patterns. The NIDA-funded research—conducted by Dr. Vivek Shetty and colleagues at the University of California, Los Angeles—was in response to the growing body of anecdotal observations and media reports about the oral health effects of methamphetamine abuse. The team of dental, addiction, and public health researchers evaluated comprehensive medical and oral health information collected from 301 adults who had received treatment for methamphetamine abuse and 301 comparable nonusers participating in the National Health and Nutrition Examination Survey III.

Increased dental disease was one of the most common health conditions among methamphetamine abusers, found in 41 percent. Methamphetamine abusers also had more teeth missing than nonusers (average 5 versus 2). People who injected methamphetamine were twice as likely to have missing teeth as smokers of the drug. Their higher rates likely reflect more severe addiction and accompanying neglect of self-care.

Dr. Shetty and colleagues concluded that dental disease is a distinctive side effect of methamphetamine abuse and that rates and patterns of dental disease may be useful in the early identification of such abuse. The study also found that 29 percent of methamphetamine abusers expressed concern about their dental appearance. Dentists may be able to use this concern to motivate stimulant abusers to participate in targeted behavioral interventions in the dental office or seek help at addiction treatment programs, the researchers say.

> Journal of the American Dental Association 141(3):307–318, 2010.

NIDA's Special Populations Office

Office Meets Dynamic Challenges of Diversity

BY LORI WHITTEN,
NIDA Notes Staff Writer

Although drug abuse touches the lives of people from all racial and ethnic backgrounds, its consequences are borne unequally. Members of minority populations often experience far worse outcomes than whites despite similar rates of addiction. Most notably, two other epidemics closely related to drug abuse—HIV infection and criminal justice involvement—are significantly higher among some racial and ethnic minorities than among other groups.

Responding to this situation, NIDA established its Special Populations Office (SPO) within the Office of the Director to coordinate research and training relevant to minority populations. Since its inception in 1993, the SPO's mission has expanded beyond racial and ethnic minorities to include other underserved groups, such as people with disabilities and residents of rural areas. The SPO promotes addiction science that examines health disparities affecting various groups and fills gaps in knowledge about drug abuse in groups that researchers have not extensively studied. Another major goal of the SPO is to foster the development of research careers among members of underrepresented communities.

DOVETAILING WITH THE DIVISIONS

The SPO developed and coordinates a strategic plan to guide the Institute's efforts to reduce addiction-related health disparities. The plan encourages NIDA Divisions and Offices to support research that:

- Determines the rates, patterns, and causes of drug abuse among minority populations;
- Develops and implements culturally specific drug abuse prevention programs, particularly in high-risk settings and hard-to-reach communities;
- Ensures the inclusion of underserved populations in treatment research and clinical trials and identifies ways to improve their treatment adherence and outcomes; and
- Applies basic and clinical neuroscience tools—for example, genetic and brain imaging studies—to identify racial and ethnic differences in vulnerability and resilience to addiction.

The SPO collaborates closely with NIDA's Divisions and other Offices as they introduce new research programs. The SPO also coordinates research that addresses disparities with a major impact on public health. For example, it hosted the African American Initiative Committee, which encouraged research on reasons and remedies for African-Americans' disproportionately high rates of HIV infection and involvement in the criminal justice system. While developing the initiative, the SPO conferred with African-American leaders and other experts on ways to better deliver HIV education, testing, counseling, and treatment in this community.

BOLSTERING INFRASTRUCTURE, EXPANDING OPPORTUNITY

One of the SPO's major goals is to strengthen the infrastructure—well-trained scientists, strong academic institutions, and knowledgeable communities—for conducting research on health disparities related to drug abuse. Infrastructure-building activities include efforts, such as mentoring of faculty and students, to improve the representation of minority scholars in addiction science. Among the core programs that the SPO manages are:

- **The Diversity-Promoting Institutions Drug Abuse Research Program**, which increases the addiction research capacity of institutions that serve students from diverse and disadvantaged backgrounds;
- **The Research Supplements to Promote Diversity in Health-Related Research Program**, which provides funding to enable existing research projects to add minority, disabled, or disadvantaged students or investigators to their teams;
- **The Special Populations Research Development Seminar Series**, in which extramural scientists and NIDA staff members offer technical assistance and information—including feedback on research ideas, NIDA priorities, and grant processes—to scientists from underrepresented groups who are poised to become independent scientific investigators;
- **Summer Research With NIDA**, which since 1997 has connected NIDA-funded scientists at more than 200 research sites with about 775 high school and undergraduate students from groups underrepresented in the biomedical and behavioral sciences; and
- **SPO-supported Minority Work Groups** of African-Americans, Hispanics, Asian-Americans/Pacific Islanders, and Native Americans/Alaska Natives, which offer essen-

STUDENTS TRY OUT ADDICTION RESEARCH CAREERS "Working in a nationally recognized lab has given me indispensable knowledge and career experience that I will be able to carry with me as I continue my studies."—Geetika Baghel, who worked with Dr. Sulie Chang at Seton Hall University in the 2009 Summer Research With NIDA program when she was a student at Piscataway High School in New Jersey.

tial community consultation for the research process. Work Group members, who are experts from outside NIDA, advise the NIDA director on minority health research and scientific development needs of their particular minority communities that will lead to effective prevention and treatment approaches. Work Group members also encourage people from their communities to enter the field of addiction research, participate in mentoring, and help development research capacity.

MEETING DYNAMIC CHALLENGES

Psychologist Dr. Lula Beatty has led the Office's efforts since its inception. She previously served in NIDA's Prevention Research Branch and conducted research at Howard University. Dr. Beatty says that since the SPO began in 1993, she has observed an increase in the number of researchers interested in addiction-related health disparities. The diversity of the research workforce has also improved: Many of the young scholars who attended SPO training workshops have succeeded in obtaining NIDA grants and now serve as faculty mentors for junior scientists. And there are more young potential researchers from special populations in the pipeline. The Summer Research With NIDA program, which attracted just 20 interested students in its first year, now draws nearly 300 applicants annually.

Many challenges remain for the SPO. "New drug problems and new health disparities constantly emerge. What's more, economic downturns and changes in the social safety net can worsen existing problems and introduce new ones," says Dr. Beatty. "However, addiction research on special populations has already led to improvements—for example, the growth in community-based drug abuse prevention." ■

Gene Influences Impact of Maternal Smoking on Children's Behavioral Problems

Genetic variants affect boys and girls differently.

BY SHARON REYNOLDS,
NIDA Notes Contributing Writer

The *MAOA* gene encodes an enzyme, monoamine oxidase A, that influences fetal brain development and regulates communication in brain circuits throughout life. NIDA-funded researchers have demonstrated that the combination of prenatal smoking exposure and specific *MAOA* genotypes increases children's and adolescents' risk for antisocial behavior.

Intriguingly, the study found that a different genotype confers susceptibility in boys than in girls. The genotype implicated among boys is the same one that other studies have associated with antisocial behavior following another adverse exposure—childhood maltreatment—among males. Among girls, psychological tests conducted in the new study suggested that the susceptible genotype and prenatal smoking exposure together promote disruptions in social information processing.

CLUES FROM PREVIOUS RESEARCH

In hypothesizing that the gene for the enzyme monoamine oxidase A (MAOA) underlies the link between prenatal smoking exposure and behavioral problems, Dr. Lauren Wakschlag of the Department of Medical Social Sciences at Northwestern University in Chicago, Illinois, and colleagues at several institutions drew upon previous findings. Research originally conducted by Drs. Avshalom Caspi and Terrie Moffit and colleagues, and since replicated in independent studies, had demonstrated that among males who experience maltreatment as children, those with the low-activity (*MAOA-L*) genotype are more likely to develop antisocial behavior than those with the high-activity (*MAOA-H*) genotype. Dr. Wakschlag's team reasoned that *MAOA* variants might similarly modify the effects of prenatal exposure to cigarettes.

To test their hypothesis, the researchers drew on their ongoing NIDA-funded East Boston Family Study, an adolescent followup to an earlier study of pregnant women, about half of whom smoked during pregnancy. Fetal exposure to smoking byproducts had been assessed by the pregnant women's repeated self-reports and blood and urine tests for cotinine, a nicotine metabolite. Together, these data provide highly accurate estimates of fetal smoking exposure, Dr. Wakschlag says.

The first adolescent followup, performed when the children were on average 15 years old, used the Diagnostic Interview Schedule for Children (C-DISC-IV) to assess symptoms of conduct disorder. About a year later, the team repeated C-DISC-IV, collected saliva for genetic analysis, and performed the Diagnostic Assessment of Nonverbal Accuracy (DANVA) to assess how well the teens could interpret the emotions expressed in pictures of faces. Finally, another year later, C-DISC-IV was performed for a third time on all the participants.

Altogether the researchers obtained full data on 176 adolescents. Roughly half the children of each sex had the *MAOA-H* genotype, and half had the *MAOA-L* genotype. The average number of conduct disorder symptoms reported per child during the entire study ranged from 0 to 15.7, with an average of 2.3. Across the three assessments, 23 percent of the boys and 7 percent of the girls met the DSM-IV three-symptom diagnostic criteria for conduct disorder.

SEX, *MAOA* VARIANTS, AND RISK

As the researchers anticipated, the mothers' smoking during pregnancy increased the risk for conduct disorder only in children with particular *MAOA* variants. Consistent with the pattern found among maltreated males, prenatal smoking exposure increased risk for boys with *MAOA-L* variants, but not for those with *MAOA-H* variants. Among girls, the reverse was true; smoking exposure increased the risk of conduct symptoms only for those with *MAOA-H* variants. These relationships remained after researchers took into account harsh parenting, parents' antisocial behavior, mothers' genotypes, and other potentially influential factors.

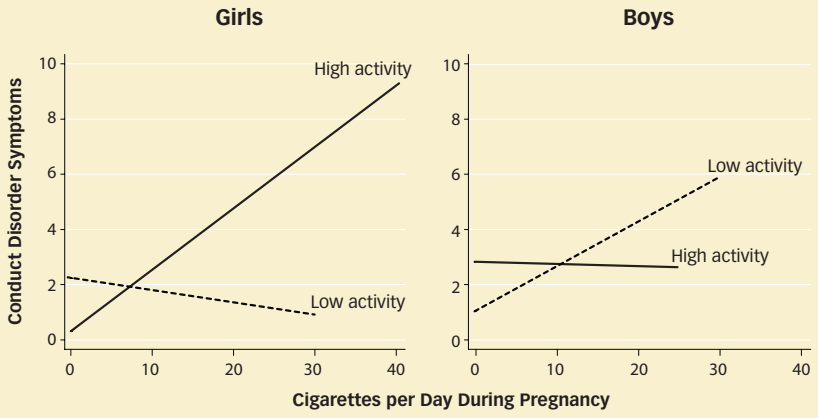
"We've now seen that a direct exposure to smoking byproducts during fetal development interacts with the *MAOA* genotype to increase risk of antisocial pathways, just as has been demonstrated with postnatal adverse social exposures, such as maltreatment," Dr. Wakschlag says. "What's critical in these findings is that they highlight, once again, the complex processes by which exposures that occur even before a child's birth interact

with genetic susceptibility to profoundly influence children's developmental trajectories."

Commenting on the study's divergent findings in boys and girls, Dr. Wakschlag says, "In research on antisocial behavior, females often get overlooked. But we really have to consider that there can be different risk processes and behavioral patterns for girls and boys."

"There's a broad interest in sex differences in brain-behavior associations, and this field of research is just beginning," says another study author, Dr. Daniel Pine of the National Institute of Mental Health. "The first thing that people will want to do is to replicate the association we observed. Assuming that it's a consistent observation, researchers will be encouraged to explore the underlying brain mechanisms."

INTERACTION OF GENE VARIANTS AND MATERNAL PRENATAL SMOKING PREDICTS CONDUCT DISORDER SYMPTOMS Behavioral symptoms, shown here as an average score based on parental reports, are associated with the mother's intensity of smoking during pregnancy only for girls having the high-activity variant of the *MAOA* gene and for boys having the low-activity variant.



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A MORE MENACING WORLD

A computer-based test of how people recognize emotions in others gave some clues as to how the *MAOA* genotype and prenatal smoking exposure might alter some children's perceptions in a way that would increase disruptive behavior. Dr. Ken Dodge and others have demonstrated that children with conduct problems often demonstrate an information-processesing style, called hostile attribution bias, in which they misperceive neutral or ambiguous situations as hostile.

In Dr. Wakschlag's study, among adolescent girls without prenatal smoking exposure, skill at identifying facial emotions was not influenced by *MAOA* variants. However, among girls with prenatal smoking exposure, those with *MAOA-H* variants tended to identify non-angry faces as angry, while girls with *MAOA-L* did not. The finding suggests that the combination of prenatal smoking exposure and the *MAOA-H* genotype biases the girls towards perceiving emotional cues as threatening. This difference was not found in boys—suggesting a fruitful avenue for further study, Dr. Wakschlag says.

"This emotion-processing bias suggests one possible mechanism by which the interaction of prenatal smoking exposure and a genetic variant increases risk of disruptive behavior. What is particularly intriguing is that this threat bias can be detected early in development, and there is some evidence that it can be altered via intervention," explains Dr. Wakschlag.

"The finding that hostile attribution is a potential mediator between the high-risk genotype and conduct disorder in girls gives us an idea of where we might target interventions," says Dr. Nicolette Borek, deputy branch chief in NIDA's Behavioral and Brain Development Branch. For these girls, training in recognizing facial expressions might be especially valuable. Further research will be required to determine information processing mechanisms by which prenatal smoking exposure and *MAOA-L* interact to influence boys' behavior.

SEROTONIN, POSSIBLY

Divergent findings in boys and girls suggest that complex biological mechanisms underline the effects of the *MAOA* genotype and prenatal smoking exposure on behavior. Potential explanations include the MAOA enzyme's role as a regulator of serotonin, a neurotransmitter that guides brain circuit formation in the developing fetus. Like the *MAOA-L* genotype, prenatal exposure to nicotine may reduce MAOA levels, and thus serotonin levels, leading to disruption in the normal growth of circuits that shape emotion and stress.

"Both prenatal nicotine exposure and *MAOA* genotype have previously been linked to conduct disorders, but researchers hadn't looked at the two together," says Dr. Borek. "Dr. Wakschlag's work provides a great opportunity to link these two things." She stresses that while this association might increase vulnerability to problem behaviors, genetics and prenatal smoking do not make future conduct problems inevitable.

Dr. Borek says that it is important to replicate these results in young children. "If we're trying to understand these interactions with an eye on designing behavioral interventions, we want to know what happens with very early behavior," she says.

Dr. Wakschlag recently received

[*Continued on page 19*]

Prison Use of Medications for Opioid Addiction Remains Low

More opioid replacement therapy in correctional facilities might yield public safety and health benefits.

BY LORI WHITTEN,
NIDA Notes Staff Writer

An estimated 200,000 people with heroin addiction pass through U.S. criminal justice systems each year, and few of them receive methadone or buprenorphine therapy. In response to a nationwide survey, prison medical directors cited doubts about the benefits of the medications, cost, concerns about the security of supplies, and longstanding institutional policies among their reasons for not offering opioid replacement therapy (ORT). Nevertheless, says Dr. Josiah D. Rich of Brown University and Miriam Hospital in Providence, Rhode Island, omitting that evidence-based approach represents a missed opportunity for improved public health and safety.

PATTERNS OF USE

Dr. Rich and colleagues approached the medical directors, their designees, or health authorities of all 50 State departments of corrections, the District of Columbia prison, and the Federal Department of Corrections—which together house more than 1.5 million inmates. Only North Dakota did not respond.

Fifty-five percent of the respondents reported that their prison systems provided methadone under some circumstances, but half gave it only to inmates who were pregnant, suffering from chronic pain, or undergoing opioid detoxification. Only 14 percent of the systems offered buprenorphine. From the survey respondents' estimated numbers of prisoners receiving the medications, Dr. Rich and colleagues calculated that only about 2,000 prisoners in the country receive ORT as an ongoing addiction treatment.

Regions of the country differed in their provision of ORT during incarceration (see map, page 9). About 64 percent of systems in the Northeast, Midwest, and West offered methadone; only 35 percent of southern systems did so. Buprenorphine therapy was common only in the Northeast, where one-third of systems offered it.

Overall, 45 percent of systems referred prisoners to methadone treatment upon release, and 29 percent made referrals to buprenorphine providers. Regionally, 78 percent of systems in the Northeast and less than half of those in the Midwest, West, and South recommended methadone programs to released inmates. The Northeast led in referrals of patients to community buprenorphine providers, with 67 percent. The percentages were less than 25 percent in the other regions.

RESPONDENTS' REASONS

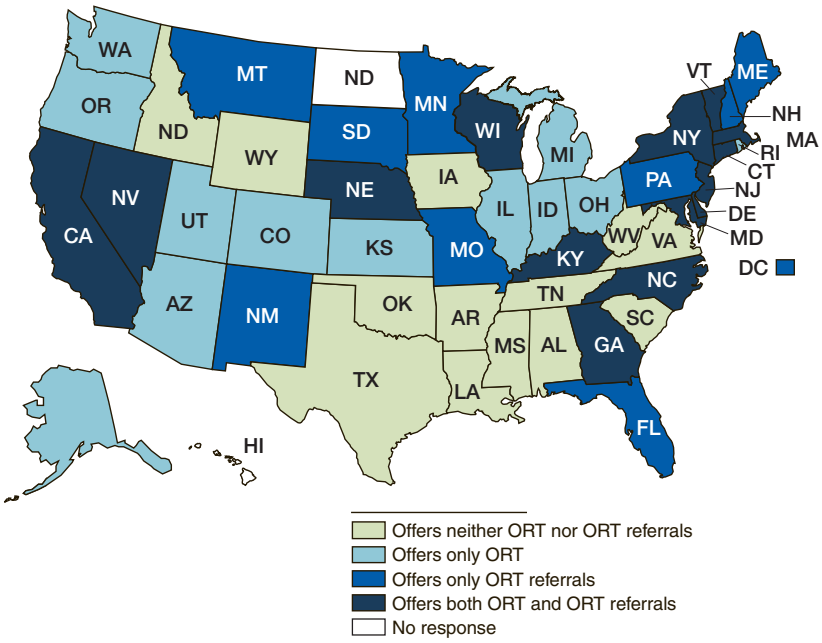
The majority of survey respondents, 57 percent, said they considered methadone to be very or somewhat beneficial for inmates with opiate addiction, and 27 percent said they did not know whether it is helpful. When asked about buprenorphine, 41 percent regarded it as useful for prisoners, and 49 percent said they did not know whether it is helpful.

Respondents from systems that did not offer ORT or post-release referrals for it gave a variety of reasons. The most common, provided by 57 percent with respect to methadone and 39 percent with respect to buprenorphine, was that the respondent favored detoxification followed by avoidance of all opioids. Some respondents cited problems that might arise from ORT regardless of whether it is beneficial for prisoners. The most frequently mentioned, by about 20 percent of respondents, was the security concern related to the supply of opioids. Other reasons included longstanding institutional policies and—for buprenorphine—cost.

Dr. Rich acknowledges that prison personnel who observe addiction primarily within the context of their institutions might question the benefits of ORT. "People working in the criminal justice system sometimes encounter individuals on methadone or buprenorphine who have been reincarcerated, and some may see this as a failure of the medication rather than viewing relapse as a symptom of a chronic disease," says Dr. Rich. "They may not see the many individuals who are stable on these medications and leading productive lives outside of prison."

Yet from a broader perspective, says Dr. Rich, studies show that prison-based ORT reduces inmates' and ex-inmates' heroin abuse, HIV transmission, and reincarceration (for example, see "Methadone Therapy in Prison Benefits Men a Year Out," *NIDA Notes,* Volume 22, Number 5, page 3). In recognition of these public health benefits, government and international agencies, including the U.S. Centers for Disease Control and

PROVISION OF ADDICTION MEDICATIONS AND REFERRALS VARIES ACROSS COUNTRY Regions differ in whether their State prisons offer opioid replacement therapy (ORT) in prison and whether they refer inmates to community facilities that provide these therapies upon release.



Adapted from the journal *Drug and Alcohol Dependence*, volume 105, numbers 1 and 2, pages 83 to 88, copyright 2009, with permission from Elsevier.

Prevention and the World Health Organization, recommend that criminal justice facilities provide ORT for prisoners. At least 30 countries, some of them low- and middle-income nations, extend ORT to prisoners.

Dr. Rich's findings suggest that more prison systems are providing methadone compared with several years ago, that the advent of buprenorphine has extended access to ORT to more inmates, and that more systems are providing referrals when prisoners are released. Nevertheless, says Dr. Rich, only a small fraction of prisoners who might benefit from ORT receive it or a referral for it.

"The results of Dr. Rich's pivotal study indicate that evidence-based treatments are not reaching a population that needs them," says Dr. Jamie Biswas of NIDA's Division of Pharmacotherapies and Medical Consequences of Drug Abuse. "The investment in pre-release addiction treatment would likely cost less than the relapse, recidivism, and family problems that stem from ongoing drug abuse."

Dr. Redonna K. Chandler of NIDA's Services Research Branch in the Division of Epidemiology, Services and Prevention Research agrees. She adds, "NIDA wants to work and talk with criminal justice professionals and decisionmakers about improving access and utilization of evidence-based therapies, including methadone maintenance." ■

SOURCE

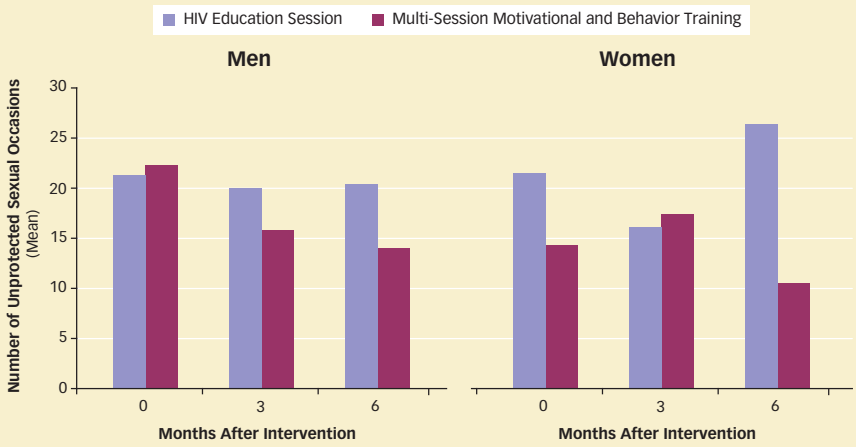
Nunn, A., et al. Methadone and buprenorphine prescribing and referral practices in U.S. prison systems: Results from a nationwide survey. *Drug and Alcohol Dependence* 105(1–2):83–88, 2009.

Intensive Interventions Reduce Risky Sexual Behaviors

Gender-specific programs designed to teach safe-sex behaviors that prevent spread of HIV prove effective among drug abuse treatment patients.

BY LAURA BONETTA
NIDA Notes Contributing Writer

REDUCING UNPROTECTED SEX Five-session behavioral and motivational training programs, specifically targeted to men or women, are more effective in reducing the number of times men and women in drug abuse treatment engage in unprotected sex than the single HIV education session typically offered at drug treatment centers. The men's program was Real Men Are Safe, and the women's program was Safer Sex Skills Building.



Multi-session motivational and behavioral training targeted specifically to men or women can cut substance abusers' high-risk sexual behaviors more effectively and enduringly than a typical single preventive educational intervention. In a large-scale test of gender-specific interventions, male participants in Real Men Are Safe (REMAS) and female participants in Safer Sex Skills Building (SSB) workshops made greater reductions in high-risk sexual behavior for a longer period than comparison groups, who were provided a standardized single-session HIV educational intervention designed to mimic those provided in many substance abuse clinics. Moreover, at the 3-month followup, men who received the training were less likely than the comparison group to have been under the influence of drugs during their most recent sexual experience.

The studies were conducted in community methadone and outpatient substance abuse treatment clinics in 10 States. All the clinics are members of NIDA's Clinical Trials Network, a partnership of academic researchers and community service providers that evaluates and adapts research-based interventions for widespread use. Staff counselors from each clinic received training by the study leaders, then delivered the interventions. "The use of staff counselors is an important aspect of these studies because it tells us that these interventions are highly feasible in real-world settings," says Dr. Susan Tross of the New York State Psychiatric Institute in New York City, who led the study of SSB.

AN AGENDA OF SELF-PROTECTION

Prevention of sexual transmission of HIV, especially among drug-abusing populations, is a critical priority for curbing the AIDS epidemic, says Dr. Donald Calsyn of the Alcohol and Drug Abuse Institute in Seattle, Washington, leader of the REMAS study. Of an estimated 56,000 new infections in 2006, the most recent year for which figures are available, 54 percent were attributed to sexual contact between men and 31 percent to heterosexual behaviors. Drug abusers and their sexual partners are disproportionately represented among people with new HIV infections.

REMAS and SSB each consists of five 90-minute sessions that teach participants about sexual transmission of HIV and other infections, identify high-risk sexual activities, and emphasize the use of safer sex practices to protect oneself and one's partners. Participants discuss concerns that they might have about using safer sex practices and engage in role-playing exercises to sharpen their negotiation skills with partners and prospective partners.

REMAS teaches the use of assertive communication and active listening skills and emphasizes taking responsibility for

protecting self and partner. SSB stresses balance between meeting relationship needs and practicing safer sex behaviors. Participants in SSB brainstorm and rehearse strategies for refusing risky sex while avoiding harm from potentially aggressive partners. "The women's intervention is oriented to communication and assertiveness and relationship skills," says Dr. Tross. "That is because, traditionally, women have not had as much power in sexual relationships as men."

GENDER-SPECIFIC PROGRAMS PROVE EFFECTIVE

Altogether 58 percent of the men and 43 percent of the women who started the REMAS or SSB programs, respectively, completed their interventions by attending three or more sessions. Participants in both groups reduced the number of unprotected sexual intercourse occasions (USOs).

Men who completed REMAS decreased these events by 21 percent from the start of the study to the 6-month followup, while men in the single HIV informational session increased USOs by 2 percent over the same period. Among women who completed the SSB program, USOs dropped by 27 percent from the start of the trial to the 6-month followup. In contrast, women who received the single HIV informational session increased their USOs by 24 percent.

REMAS was particularly effective in inculcating condom use during sex with casual partners. The percentage of REMAS recipients reporting such use during 80 percent or more of sexual encounters increased from 4 percent before the intervention to 20 percent at the 6-month followup.

The REMAS goal of reducing men's drug use during sexual activity was achieved in the short run: Whereas prior to the intervention, 36.8 percent of REMAS recipients reported being under the influence of drugs during their most recent sexual encounter, that percentage fell to 25.7 at the 3-month followup. For men who received only the single session of HIV information, drug use rose over the same interval from 36.9 percent to 38.3 percent. After 6 months, the groups were similar with about 31 percent of each group reporting sex under drug influence during their most recent sexual event.

Says Dr. Calsyn, "We would like to see drug treatment centers start to adopt HIV-preventive interventions that are designed for substance abuse patients and go beyond the information provided in one-session interventions."

"The good news is that if you can do the SSB program, you not only get immediate benefits in women avoiding unprotected sex, but the benefits can hold for at least 6 months," says Dr. Tross. "That is the great challenge for safer sex in the HIV era: You have to change the behavior not just once but for the long haul."

The Centers for Disease Control and Prevention (CDC) has placed both REMAS and SSB in its database of interventions that scientifically rigorous studies have established as being highly effective. "Being on the CDC list means that these interventions will be disseminated on a much larger scale than if they were just published in a journal article," says Dr. Jacques Normand, director of NIDA's AIDS Research Program.

"These studies are important because they tackle sexual risk behavior," says Dr. Normand. "Up until recently, HIV prevention for substance abusers concentrated on reducing injection-related risk behavior, but NIDA is now supporting studies that pay attention to sexual risk behavior in the context of substance abuse."

For detailed descriptions of the interventions and free manuals and implementation aids regarding REMAS, see *ctndisseminationlibrary.org/display/397.htm;* for SSB, see *ctndisseminationlibrary.org/display/398.htm.* ■

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Calsyn, D.A., et al. Motivational and skills training HIV/sexually transmitted infection sexual risk reduction groups for men. *Journal of Substance Abuse Treatment* 37(2):138–150, 2009.

Tross, S. Effectiveness of HIV/STD sexual risk reduction groups for women in substance abuse treatment programs: Results of NIDA Clinical Trials Network Trial. *Journal of Acquired Immune Deficiency Syndrome* 48(5): 581–589, 2008.

[*Continued from page 1*]

lever twice as many times as the second group before the effort needed to obtain the drug outweighed their drive for it.

Dr. Rodrigo España and colleagues at Wake Forest University (WFU) in Winston-Salem, North Carolina, independently conducted progressive ratio trials. Their results were similar to those of the UBC–UCSF team. In further experiments, the WFU team produced additional evidence that orexin comes into play as a motivator specifically when the cost of cocaine rises. They showed that:

- In a fixed ratio trial, where the work required to maintain a preferred blood concentration of cocaine remained low and constant, rats with normal and blocked orexin-1 receptors self-administered roughly equal amounts of cocaine.
- However, in a protocol that progressively escalated the amount of work necessary to maintain a preferred blood concentration, rats with normally functioning orexin receptors worked about 40 percent harder than rats with blocked receptors.

RESPONSIVENESS TO COCAINE CUES

Drs. Gary Aston-Jones, Rachel Smith, Pouya Tahsil-Fahadan, and colleagues at the Medical University of South Carolina (MUSC) demonstrated that orexin increases rats' responsiveness to stimuli that accompany drug taking. Their work suggests that the neuropeptide may contribute to risk for relapse when recovering individuals encounter people, places, or things that they associate with drug use.

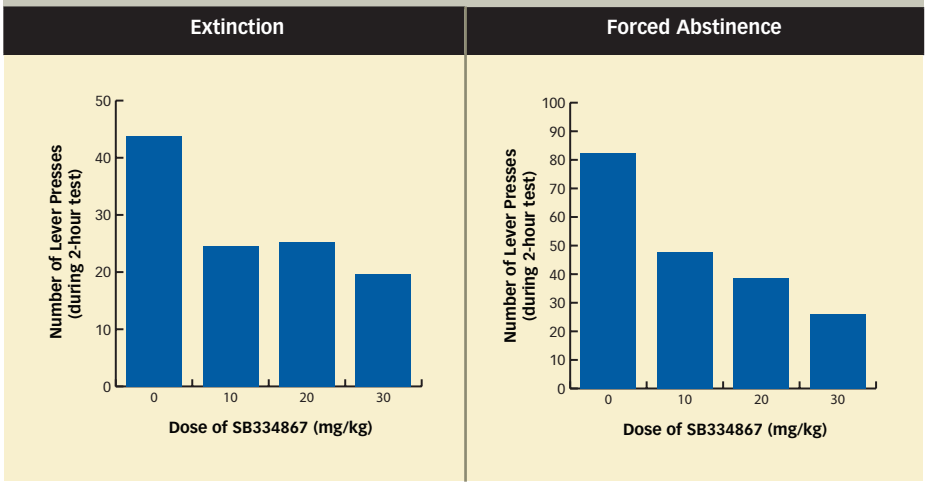
In one experiment, Dr. Aston-Jones and colleagues trained rats to press a lever to self-administer cocaine and to associate the experience with sound and light cues. They then deactivated the lever and cues. This phase of the protocol, called extinction training, weakened the animals' drug-lever association to the point where they stopped pressing the lever, but it left their drug-cue association intact. Finally, the researchers re-exposed the animals to the cues. Typically in experiments with addictive drugs, such re-exposure will reactivate animals' drug-lever associations and prompt them to resume avid lever pressing. In the MUSC experiment, rats with normal orexin function did just that, but animals that had been treated with SB334867 did not.

The neuropeptide may contribute to risk for relapse when recovering individuals encounter people, places, or things that they associate with drug use.

Another MUSC experiment more closely resembled the situation of drug abusers who become abstinent outside of their home communities and then return to them. Rats self-administered cocaine in a cage with distinctive visual, auditory, olfactory, and sensory features—for example, a tone of a particular pitch, lemon scent, and mesh floor. This environment provided the animals with drug associations that had some of the richness and complexity of those experienced by drug abusers. When returned to this self-administration cage after extinction training in another cage, normal animals pressed the lever significantly more than those with blocked orexin-1 receptors.

The MUSC team designed another experiment to more closely approximate drug abusers' experience in a different respect. In contrast to animals that undergo extinction training, Dr. Aston-Jones notes, "Most drug-dependent individuals are not explicitly trained that an environment no longer offers drugs." With this in mind, the researchers trained rats to self-administer cocaine in a test cage, then moved them to another cage with no extinction training and no access to cocaine for 2 weeks. When the animals were returned to the test cage, those that were normal pressed its (now deactivated) lever 83 times in a 2-hour session, compared with 26 presses by animals whose orexin-1 receptors had been blocked with 30 mg/kg of SB334867.

DIFFERENT MODELS OF RELAPSE REVEAL RECEPTOR BLOCKER'S EFFECT When returned to a chamber in which they previously self-administered cocaine, rats that had received the orexin-1 receptor blocker SB334867 sought the drug less avidly than those that had received an inert substance. Blocking orexin receptors reduced rats' drug seeking regardless of whether the animals had learned that an environment no longer offered cocaine (extinction training) or simply had not had access to the drug (forced abstinence).



ONE MEDICATION FOR TWO COMPULSIONS?

To the UBC–UCSF and WFU researchers, their results suggested that orexin supplies the extra motivational salience that distinguishes high-impact rewards, such as cocaine provides, from normal rewards. To confirm this hypothesis, they conducted experiments with another type of substance that many people consume to the detriment of their health: delectable high-calorie food.

Drs. Borgland and Bonci and colleagues again used progressive-ratio protocols, now with either high-fat chocolate or ordinary rat chow as rewards. The results with chocolate paralleled those with the drug: Rats that received SB334867 put in less effort than rats with normal orexin signaling. In contrast, animals with normal signaling and those with blocked orexin-1 receptors worked equally hard for chow (see graph). Similarly, when the researchers gave animals the option of climbing over a 30-cm-high wall to get chocolate or simply walking to an open bin of chow (see diagram, page 1), animals with normal orexin chose the harder path more often.

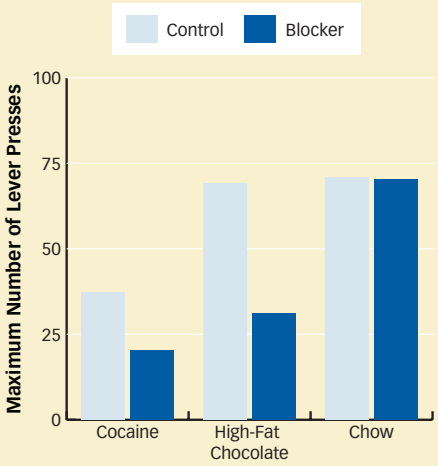
Dr. España and colleagues conducted an experiment that suggests that orexin is part of the answer to the question: Why are sweets in the afternoon more likely to ruin our appetite for dinner than dinner is to make us pass up dessert? They found that orexin increases animals' drive for sugar pellets when they are well-fed, but not when they are hungry (see box, right).

Dr. Bonci, who is now scientific director of NIDA's Intramural Research Program, says that all these results encourage investigation of orexin-1 receptor blockade as a potential treatment for both cocaine addiction and overeating. "Blocking orexin-1 receptors does not appear to dampen all motivation [which would be undesirable], but it would put the brakes on drives for high-impact rewards that evoke pathological consumption."

Dr. Aston-Jones adds, "Patients taking an orexin-1 blocker to treat cocaine abuse would probably continue to, for example, enjoy normal food because the blocker seems to selectively influence highly salient rewards—ones with high significance either because of biological properties or through conditioning."

Dr. Susan Volman of NIDA's Division of Basic Neuroscience and Behavioral Research comments, "These converging findings from three laboratories suggest that signaling at orexin-1 receptors influences the ability of highly salient rewards to drive compulsive behavior. Additional research on the cellular pathways underly-

OREXIN-1 RECEPTOR REGULATES DRIVE FOR COCAINE AND CHOCOLATE Rats that received an orexin-1 receptor blocker gave up seeking high-impact rewards—cocaine and chocolate—after fewer lever presses than those in a control group that received an inert substance. The blocker did not alter rats' motivation for standard chow. In the experiments with food, rats were only slightly hungry during the test.



Orexin, Appetite, and Obesity

Dr. Rodrigo España and colleagues at Wake Forest University (WFU) produced evidence suggesting that signaling at orexin-1 receptors does not have a role in eating to meet nutritional needs, but it is required for well-fed animals to seek sugar. This finding is consistent with others that have made inhibiting orexin-1 receptor signaling a candidate strategy for treating uncontrolled eating that leads to obesity.

The WFU researchers compared hungry and sated rats' willingness to work for sucrose pellets in two tests, one with normal orexin-1 receptor signaling and one after treatment with the orexin-1 receptor blocker, SB334867. The hungry animals, which had been allowed access to chow for only 1 hour per day prior to the trials, worked equally hard for sucrose pellets regardless of their orexin status. However, the sated animals, which had eaten their fill of chow prior to the trials, worked to obtain about 1.5 times as many sugar pellets when their orexin signaling was normal as they did when the neuropeptide's activity was blocked.

SOURCE

España, R.A., et al. The hypocretin-orexin system regulates cocaine self-administration via actions on the mesolimbic dopamine system. *European Journal of Neuroscience* 31(2):336–348, 2010.

Orexin's Neural Underpinnings

Two research teams traced orexin's motivational effects to its influence on dopamine neurons in the brain's reward pathway. Stimulation of the orexin-1 receptor, they found, mediates the superabundant dopamine release that enhances the impact of cocaine and other compulsively sought rewards.

Dr. Rodrigo España and colleagues at Wake Forest University in Winston-Salem, North Carolina, demonstrated that orexin neurotransmission mediates dopamine release following cocaine exposure. After an intravenous infusion of cocaine, dopamine levels rose significantly higher in a key reward area, the nucleus accumbens (NAc), in animals with normal orexin neurotransmission than in animals with blocked orexin-1 receptors.

Dr. Stephanie Borgland of the University of British Columbia, Dr. Antonello Bonci of the University of California, San Francisco, and colleagues shed light on how orexin enhances dopamine release. They found that among rats exposed to either cocaine or high-fat food—but not less rewarding substances—dopamine neurons in the ventral tegmental area showed increased activity in response to orexin. Enhanced bursts of activity in the presence of orexin would increase dopamine release in the NAc. This work built on prior research by Dr. Gary Aston-Jones and colleagues at the Medical University of South Carolina that first reported a link between orexin and reward. They demonstrated that microinjections of orexin into the ventral tegmental area of rats induce a return to drug seeking (see "Neuropeptide Promotes Drug-Seeking and Craving in Rats," *NIDA Notes*, Volume 21, Number 4, page 1).

"My colleagues and I hypothesize that when a highly salient reward is present, the orexin system kicks into play and increases dopamine release in the neurons of the reward pathway," explains Dr. Borgland. "It would follow that after administration of an orexin-1 receptor blocker, cells would be less likely to release dopamine in response to a reward—and that would make the reward less motivating."

Considering the potential use of orexin-1 blocking medications to help individuals overcome cocaine craving, Dr. España says, "Virtually all drugs of abuse cause a surge of dopamine in the brain's reward pathway, but medications that directly inhibit dopamine stifle motivation for normal behavior. Dampening dopamine indirectly with medications that block orexin receptors is a more promising strategy."

ing orexin's effect on motivated behaviors will likely advance medication development efforts." ■

SOURCES

España, R.A., et al. The hypocretin-orexin system regulates cocaine self-administration via actions on the mesolimbic dopamine system. *European Journal of Neuroscience* 31(2):336–348, 2010.

Smith, R.J.; Tahsili-Fahadan, P.; and Aston-Jones, G. Orexin/hypocretin is necessary for context-driven cocaine-seeking. *Neuropharmacology* 58(1):179–184, 2010.

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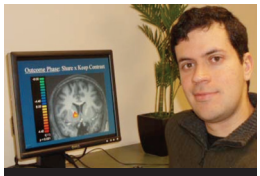
Smith, R.J.; See, R.E.; and Aston-Jones, G. Orexin/hypocretin signaling at the orexin 1 receptor regulates cue-elicited cocaine-seeking. *European Journal of Neuroscience* 30(3):493–503, 2009.

Grantee Wins Early Career Award



Dr. Mauricio R. Delgado of Rutgers University in Newark.

NIDA grantee Dr. Mauricio R. Delgado of Rutgers University in Newark, New Jersey, received a 2010 Presidential Early Career Award for Scientists and Engineers (PECASE). He was one of 85 researchers recognized for their accomplishments by President Barack Obama last November. Dr. Delgado and his team use functional magnetic resonance imaging to investigate how the human brain learns from positive and negative experiences and how this information guides behaviors associated with drug addiction.

"Science and technology have long been at the core of America's economic strength and global leadership," President Obama said in presenting the PECASE awards. "I am confident that these individuals, who have shown such tremendous promise so early in their careers, will go on to make breakthroughs and discoveries that will continue to move our Nation forward in the years ahead."

Each year, 10 Federal departments and agencies nominate meritorious scientists and engineers whose early accomplishments show great promise for maintaining America's preeminence in science and engineering. Winners receive research grant extensions for up to 5 years to further their studies in support of critical government missions.

NIDA Cosponsors Mentoring Service for Clinicians Advising Substance-Abusing Patients

With a free phone call or email, primary care clinicians can tap a mentor for help with a sensitive subject: how to address alcohol, tobacco, and drug abuse among patients. The mentor—an expert in primary care and addiction medicine—advises on screening, brief interventions, and treatment in primary care settings. This service, Physician Clinical Support System for Primary Care (PCSS-P), also offers resources to registered participants for incorporating screening and followup into regular patient care. PCSS-P is a project of NIDA and the American Society of Addiction Medicine (ASAM).

The free "warm line" service provides a response within 24 hours rather than the immediate response that is characteristic of hotlines. The service extends the Institute's NIDA**MED** initiative, which stresses the importance of the patient-doctor relationship in identifying unhealthy behaviors before they evolve into life-threatening conditions. To take advantage of the service, physicians can call PCSS-P at 877-630-8812 or register online at *www.PCSSmentor.org*. NIDA**MED** resources include a screening tool, quick reference guide, and comprehensive resource guide for clinicians. NIDA**MED** resources can be found at *www.nida.nih.gov/nidamed/*.

Week-Long Events Teach Teens Drug Abuse Facts

Daevion Caves and Jordan Atkins won first place in the Awareness Through Music Contest.

With NIDA's encouragement and support, local communities and organizations in more than 20 States sponsored events to educate teenagers about drugs and drug abuse during the Institute's first annual National Drug Facts Week, held November 8–14.

NIDA's outreach efforts helped spark more than 90 community-based events, including town meetings, symposia, Web activities, TV programs, and contests. Sponsors included schools, community groups, sports clubs, book clubs, and local hospitals. NIDA provided an online toolkit that helped sponsoring organizations plan and publicize their events and find experts and scientific information on drugs.

The week's events included:

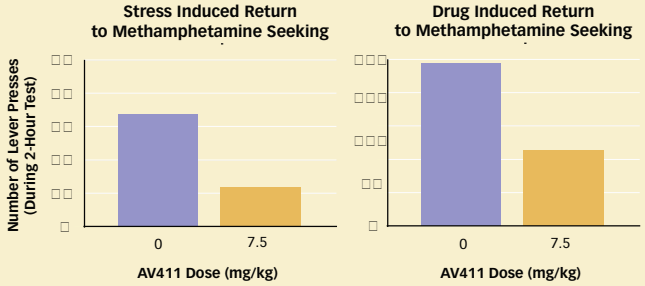
- NIDA's fourth annual **Drug Facts Chat Day**, during which scientists from NIDA gathered in Bethesda, Maryland, to answer almost 1,600 online queries about drugs and drug abuse from middle and high school students. Seventy-five schools registered for the 2010 Chat Day, including one in Rome, Italy. Students most frequently asked questions about marijuana, alcohol, nicotine, and prescription drugs. For the first time, representatives from the National Institute on Alcohol Abuse and Alcoholism and the National Institute of Mental Health participated in Chat Day discussions.
- A Teen Substance Abuse **Awareness Through Music Contest**, in which high school students created and performed an original song, music video, or combination of the two depicting the dangers of drug abuse or celebrating a healthy lifestyle. Two boys from Alton High School in Alton, Illinois—18-year-old Daevion Caves and 16-year-old Jordan Atkins—won first place for their music video entitled "Drug Free State of Mind." MusiCares and the GRAMMY Foundation cosponsored the contest, in collaboration with NIDA. NIDA is accepting entries for this year's contest until October 10, 2011. For more information, visit *drugfactsweek.drugabuse.gov*.

Further information about National Drug Facts Week events is posted at *drugabuse.gov/list/2010/public017.html*. The next National Drug Facts Week will begin October 31, 2011. ■

Medication Reduces Rats' Return to Methamphetamine Seeking

A new medication strategy shows promise for preventing relapse to drug abuse, new animal research suggests. Dr. Patrick M. Beardsley at Virginia Commonwealth University, Dr. Kirk Johnson at MediciNova, Inc., and colleagues demonstrated that AV411 (also called ibudilast) reduced methamphetamine seeking in animal models of stress- and drug-induced relapse. Prior work by Dr. Linda Watkins, Dr. Johnson, and colleagues had indicated that AV411 acts as a potent pain reliever while having minimal abuse potential. Other preliminary tests by the Watkins-Johnson team suggest that AV411 reduces the rewards associated with morphine—hinting at the medication's potential as an anti-addiction therapy as well as an analgesic (see "AV411 for Pain Relief Without Opioid Side Effects," *NIDA Notes*, Volume 22, Number 1, page 12).

MEDICATION ATTENUATES RETURN TO DRUG SEEKING IN RATS Rats that received the medication AV411 sought methamphetamine less avidly in response to either a stressor or a small dose of methamphetamine than those in a control group.



To evaluate AV411 as a potential relapse medication, Dr. Beardsley trained rats to press levers for methamphetamine self-infusion and then stopped delivering the drug. The rats responded with reduced rates of lever-pressing. When the rats then experienced stress, such as a mild foot shock, or a small injection of methamphetamine, they resumed their high rates of lever pressing, which are considered a sign of relapse. However, if rats were treated with AV411 when their access to methamphetamine self-administration was removed, drug-seeking was significantly reduced in both stressed rats and rats that had received the priming injection (see graph).

AV411 is of special interest to drug developers because, unlike most anti-addiction medications, AV411 affects the brain's glial cells rather than neurons. This different mode of action may avoid side effects caused by other anti-addiction medications.

AV411 is prescribed in Asia to treat asthma and post-stroke dizziness, and it is being tested in Eastern Europe for treatment of multiple sclerosis and in the United States for other neurological conditions. In all of these uses, it has established a good safety profile.

European Journal of Pharmacology 637(1–3):102–108, 2010.

Computer-Based Intervention Offers Good Value for Money

NIDA-funded researchers have for the first time demonstrated the economic value of a computer-based treatment as an adjunct to standard addiction therapy. Dr. Todd Olmstead of George Mason University and colleagues determined that adding Computer-Based Training for Cognitive-Behavioral Therapy (CBT4CBT) to standard care resulted in an expense of $21 for each additional drug-free urine. This compares favorably with the cost-effectiveness of other evidence-based addiction therapies. For example, prior research found that the clinic cost per additional drug-free urine obtained by adding prize-based contingency management to methadone maintenance was $70.

Dr. Olmstead analyzed data from a randomized trial led by Dr. Kathleen Carroll of Yale University. That trial demonstrated that adding twice-weekly access to CBT4CBT to the usual treatment helped patients at community clinics stay abstinent longer than the usual treatment alone (see "Computer-Based Interventions Promote Drug Abstinence," *NIDA Notes*, Volume 22, Number 5, page 1). The program closely follows the content and session structure of cognitive-behavioral therapy (CBT), an evidence-based treatment for addiction. The manual for CBT is available through the NIDA Web site (*archives.drugabuse.gov/TXManuals/CBT/CBT1.html*).

Although other researchers have demonstrated that computer-assisted delivery of cognitive-behavioral therapy offers good value in treatment of anxiety and depression, experts had not conducted cost-effectiveness analyses for computer-assisted addiction therapies. The new findings of Dr. Olmstead and colleagues suggest that CBT4CBT may be a cost-effective way to expand access to CBT for addiction. Moreover, if the CBT4CBT program remains effective when patients use it from a home computer or over the Internet, the value and reach of this e-therapy may expand dramatically.

Drug and Alcohol Dependence 110(3):200–207, 2010.

VOLUME 23 INDEX

Issue number appears in parentheses, followed by page number(s).

GENE INFLUENCES

[*Continued from page 7*]

NIDA funding to replicate and extend this research to early childhood. She and Dr. Kimberly Andrews Espy, a developmental cognitive neuroscientist at the University of Nebraska, Lincoln, and colleagues with expertise in molecular, statistical, and behavior genetics are conducting an intensive, preschool-age followup of children of women who participated when pregnant in a NIDA-funded study led by Dr. Espy.

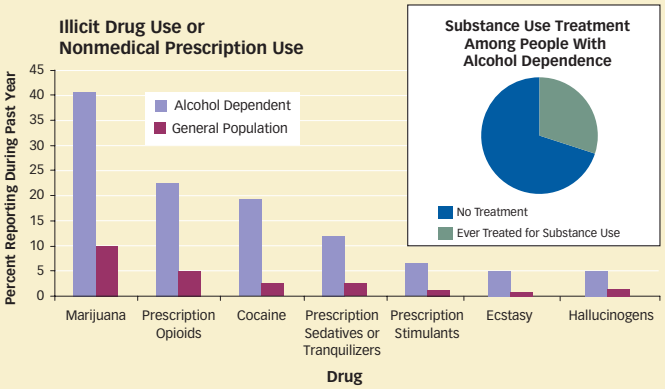
The new project uses measurements of behavior and neurocognition that the researchers specifically developed for preschoolers. In addition to employing two complementary genetic approaches, the study will apply measures of brain reactivity to subgroups of exposed and nonexposed children. Dr. Espy says, "We hope to explicate the complex pathways from genes to brain to behavior and gain a much more precise understanding of the impact of prenatal tobacco exposure across development. The study design will allow us to elucidate the role of prenatal tobacco exposure in the complex and dynamic gene-environment milieu." ■

SOURCE

Wakschlag, L.S., et al. Interaction of prenatal exposure to cigarettes and *MAOA* genotype in pathways to youth antisocial behavior. *Molecular Psychiatry*. 15(9): 928–937, 2010.

WHAT THE NUMBERS SAY

High Rates of Illegal Drug Use Among Alcohol-Dependent Adults



Adults dependent on alcohol report high rates of illegal drug use and nonmedical use of prescription drugs, as compared with the general population. Seventy percent of those with alcohol dependence had never received treatment for that problem or other substance abuse.

Sources: Hedden, S.L., et al. Patterns of illegal drug use among an adult alcohol dependent population: Results from the National Survey on Drug Use and Health. *Drug and Alcohol Dependence* 106(2–3):119–125, 2010; and comparison data for the general population aged 18 or older from the 2007 NSDUH (*oas.samhsa.gov/NSDUH/2k7NSDUH/tabs/Sect8peTabs1to42.htm#Tab8.14B)*.

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